THE NUTRITIVE VALUE AND PHYSIOLOGICAL EFFECTS OF XYLOSE UPON ORAL ADMINISTRATION TO THE ALBINO RAT

BY

ZOE ESTELLE ANDERSON

B.S.A.S., Lewis Institute, 1939
M.S., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN ANIMAL NUTRITION
IN THE GRADUATE COLLEGE OF THE
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THE NUTRITIVE VALUE AND PHYSIOLOGICAL EFFECTS OF XYLOSE UPON ORAL ADMINISTRATION TO THE ALBINO RAT

Most of the investigations on the possible nutritive value of xylose have been based on the theory that any utilizable carbohydrate must go through the normal metabolic pathway for the oxidation of carbohydrates, first being changed to glucose and then passing through the citric acid cycle to carbon dioxide and water. If oxidation does not take place immediately, the glucose formed may be stored as liver or body glycogen, or more permanently as fat. If oxidation does take place, the respiratory quotient of the animal should approach unity. Continuing further with this theory, if glucose is formed from an ingested foodstuff, the blood level of glucose should rise.

In 1905, Pflüger criticized the older work reporting the formation of glycogen from pentoses and concluded there was no experimental evidence available to support the belief that pentoses could give rise to glycogen in the animal body. Subsequent to Pflüger's publication, there has appeared conflicting evidence on the formation of glycogen from administered pentoses.

No glycogen formation was observed by Brasch ('08) after oral administration of rhamnose, arabinose, or xylose. He employed dogs and rabbits as experimental animals. Liver and muscle glycogen was reported to increase in frogs which had received arabinose and xylose (Thomas et al '29). Nitzescu and Benetato ('29) reported the assimilation and utilization of pentoses by rabbits. They based their conclusions on increased glycogen in liver and muscle tissue and a decreased total nitrogen in the urine after administration of rhamnose, arabinose, and xylose. All of these investigators neglected

to study the problem of absorption. Their experimental procedures and doses varied.

Cori ('25) established the fact that a monosaccharide is absorbed from the intestines of the rat at a constant rate, specific for the sugar, and unrelated to its concentration. Galactose is the most rapidly absorbed and the others are absorbed less rapidly in the following descending order: glucose, fructose, mannose, xylose, and arabinose.

Miller and Lewis (p. 133, 141, '32) showed that no increase in liver or body glycogen was evident three hours after administering 2 c.c. of a 50 per cent solution of xylose by stomach tube. This was substantiated in the report of the Blatherwick group ('36) who also found no change in the amounts of lactic acid in liver, muscle, or blood. They did find that blood glucose was raised significantly by the administration of xylose, and that this increase could not be entirely accounted for by a change in blood volume. The rise in blood glucose following introduction of xylose into the animal body had been reported by Blanco ('32). Failure of formation of glycogen or lactic acid from xylose is very strong evidence that there is little or no oxidation of xylose but is weakened by the fact of an increase in blood glucose. The possibility remains that the extra glucose in the blood may have had its origin in the administered xylose.

Determination of respiratory quotient after feeding was employed as a method of study of this problem by Marble and Strieck ('32). Following forced feeding of 30 grams of xylose in 100 c.c. of water, an increase in respiratory quotient occurred in both normal and phlorizin-diabetic dogs. A similar increase followed administration of this sugar to normal and diabetic humans, measurement being made by direct calorimetry. The dynamic effect was slight and of short duration, in no case greater than 15 per cent. Alkali reserve was simultaneously determined by the Van Slyke method. The results demonstrated that the increase in respiratory quotient was due to oxidation and not to a flushing out of carbon dioxide. The authors conclude that oxidation had taken place

but not to any great extent. The increase of the respiratory quotient toward unity indicates that whatever oxidation may have taken place was through the metabolic pathway of carbohydrates.

A number of investigators have studied the excretion of xylose. No one has succeded in quantitatively recovering xylose in the excreta. When xylose is taken by a normal man, about one-third is excreted in eight hours at which time excretion is apparently ended (Blatherwich et al '36). Failure of excretion strongly suggests some utilization.

The intestional disturbances resulting from the ingestion of xylose have been reported by a number of investigators. Some laxatives include xylose for its diahrretic effect. A reversible albuminous degeneration of liver and kidney tissue following the administration of xylose was observed by the Blatherwich group ('36).

There is no clear cut demonstration in the literature that no energy is available to the monogastric animal from xylose. There is likewise no clear cut evidence that it does supply energy. Indeed, most of the evidence points to failure of its oxidation. The feeding of fats does not result in increased blood glucose, increased liver or body glycogen, increased respiratory quotient, yet their energy value is unquestionable. Is it justifiable to conclude there is no utilization of the monogastric animal of potential energy available to some species of organism without making measurements in terms of energy?

Tests carried out in the Animal Nutrition Laboratory at the University of Illinois (Shehata '47, unpublished) indicate the nutritive value of xylose, when fed to the albino rat, is greater than that of woodflock but less than that of glucose.

The purpose of this study was to establish whether or not xylose has any nutritive value to the monogastric animal and to record the physiological effects of the feeding of varying levels of this sugar to the albino rat.

Seven separate experiments were carried out in the labora-

tory, for problems encountered necessitated the need for further work.

Methods

(1) *Experiment One:* Albino rats were pair fed otherwise equal diets containing 39.4 per cent of glucose or xylose. Gains were kept equal by addition of measured quantities of glucose added to the diet of the rats receiving xylose. Grams of glucose per gram of gain was calculated for each diet as a measure of the energy value of xylose in proportion to the energy value of glucose. Activity was measured.

(2) *Experiment Two:* Comparison was made of the nitrogen sparing effect of xylose, glucose, and sucrose.

(3) *Experiment Three:* The toxicity of xylose was determined at different dietary levels.

(4) *Experiment Four:* Survival of rats receiving only xylose and water was compared with those receiving only water or glucose and water.

(5) *Experiment Five:* Measurement was made of the voluntary activity of rats following oral and intraperitioneal administration, to determine if the cause for reduced activity upon the ingestion of xylose was a measure of the toxicity due to its metabolic presence or was due to intestinal disturbance.

(6) *Experiment Six:* Comparison was made of liver glycogen following the administration of water, xylose, and glucose.

(7) *Experiment Seven:* Comparison was made of energy and nitrogen gains of rats pair fed diets varying only in that one pairmate received xylose and the other glucose. Energy, nitrogen, and xylose balance studies were run during a portion of the experimental feeding period. Heat production of the rats was determined as was also the heat increment of the two diets and of the two sugars being compared. All calcula-

tions were based on values obtained by chemical analysis. Rats were closely confined.

Physiological observations accompanied each experiment. All experimental rats were housed in a constant temperature room at 78 degrees F. throughout all testing periods.

Results

The evidence obtained in these seven experiments is combined in the following discussion:

1. The administration of xylose, whether by oral or intraperitoneal route, results in a highly significant reduction of voluntary activity, even when the quantity administered is equal to only 10 per cent of the ration. The effect is immediate and continues during a prolonged feeding period.

When voluntary activity was measured in revolving cages:

(a) Eleven male rats receiving 39.4 per cent xylose showed a lesser activity than pair mates fed 39.4 per cent glucose. The mean difference between pairs was equal to 193 ± 35 revolutions per hour, $p = 0.002$.

(b) Eight male rats receiving xylose equal to 10 per cent of their ration showed a decreased voluntary activity of 20.2 ± 12.6 per cent from a control period.

(c) Eight male rats receiving intraperitioneal injection of xylose equal to 10 per cent of their ration showed a decreased voluntary activity of 54.6 ± 4.6 per cent from a control period. When injected with distilled water alone, the mean decrease in voluntary activity was only 11.0 ± 13.4 per cent.

The depression of voluntary activity is evidently the result of the metabolic presence of a foreign sugar which interferes with normal metabolism and creates a reversible albuminous degeneration of liver and kidney tissue, causing the liver cells to become granular and swollen and the whole organ to hyper-

trophy. Activity is suggested as a sensative measure of toxicity of a substance in the absence of gross evidence.

2. Ingestion of xylose creates digestive disturbance evident by a severe diarrhea and bloat. The diarrhea subsides with time, depending upon the quantity being ingested.

3. Voluntary food intake is reduced as the per cent of xylose in the ration is increased.

4. The dietary presence of xylose reduces the efficiency of the utilization of protein by the albino rat.

(a) Nine male albino rats fed a low protein diet excreted more nitrogen when 45 per cent xylose was present in the diet than when the xylose was replaced with either glucose or sucrose. Mean values for milligrams of nitrogen retained per gram of nitrogen ingested were: 7.62 ± 0.5 on the 45 per cent xylose diet: 11.16 ± 0.003 on the 45 per cent glucose diet: and 10.93 ± 0.8 on the 45 per cent sucrose diet. The difference between the values for the glucose and xylose diets was highly significant, $p = 0.0003$. Comparing the sucrose and xylose diets, $p = 0.0063$, which is also highly significant.

(b) The body lengths of rats fed 39.4 per cent xylose was significantly less than the body lengths of those fed 39.4 per cent glucose.

(c) Balance studies revealed more nitrogen in the feces in the presence of dietary xylose. When eight female and seven male rats were pair fed 20 per cent xylose rations versus 20 per cent glucose rations, a mean value of 0.014 grams more nitrogen per day was excreted by the rats receiving xylose, $p = 0.0133$ for the females, and $p = 0.0001$ for the males. There was no significant difference in the urinary nitrogen excretion of the females. The male rats ingesting xylose excreted a mean of 0.0196 grams more nitrogen per day than their pair mates, $p = 0.0064$.

The female rats showed a greater gain in total nitrogen on the glucose diet. A mean value of 0.302 ± 0.123 grams

more nitrogen was deposited on the 20 per cent glucose ration than on the 20 per cent xylose ration, $p = 0.0105$. There was no consistent difference in the nitrogen gains of the male rats. The mean difference between pair mates was 0.043 ± 0.13 grams of total nitrogen, $p = 0.2014$.

5. The energy of xylose is not available to the young albino rat for growth when fed as 20 per cent of a ration adequate in other respects. Measurement was made of gains in terms of Calories consumed per Calorie gained by determination of the energy of the rations and of the rat carcasses after pair feeding 30 experimental animals for a period of 47 to 67 days on rations containing 20 per cent xylose versus 20 per cent glucose. There was no significant difference in Calories consumed per Calorie gained when the energy of the xylose was excluded from the calculations. The rats fed the xylose ration consumed 0.258 ± 0.322 more non-xylose Calories than did their pair mates, $p = 0.4688$. Any possible difference in the maintenance requirement of the animals, due either to activity or body size, would be in the direction of a greater requirement by those receiving the glucose diet. This fact strengthens the evidence that the rats were unable to utilize the energy of xylose.

6. Administration of xylose by stomach tube did not increase liver glycogen. The mean values obtained for milligrams of glucose per gram of liver were: 4.39 ± 1.80 in eight fasting rats given 2 c.c. of distilled water; 16.33 ± 1.95 in nine fasting rats given 2 c.c. of a 50 per cent solution of glucose; and 4.34 ± 1.69 in nine fasting rats given 2 c.c. of a 50 per cent solution of xylose.

7. Ingestion of xylose by starving rats prolonged life by approximately 4 days. The difference was significant. Decreased activity of the rats or alteration of the sugar to a utilizable fatty acid by the intestinal flora was the most probable explanations of the slight increase in survival.

8. Basal metabolism of 16 female rats pair fed 20 per cent xylose versus 20 per cent glucose diets averaged 7.18 ± 14.10

Calories per square meter of body surface area per day. This value is very close to that obtained by Mitchell and Carman ('26) when calculated on the same basis, that of Lee's formula ('29). There was no significant difference in the basal metabolic rate of the pair mates.

No significant difference was observed in the fasting confined metabolism measured on eleven male and sixteen female rats pair fed 20 per cent xylose and 20 per cent glucose diets. The incidental activity of the rats during 4 to 6 hours in the Haldane gravimetric apparatus increased heat production approximately 20 per cent over the basal heat production.

No difference was observed in the heat increment of two rations containing 20 per cent xylose and 20 per cent glucose. The extra Calories of heat production resulting from the ingestion of the 20 per cent glucose diet was 0.5291 and from the 20 per cent xylose diet was 0.3732, $p = 0.1945$. There was no evidence that xylose alone has a greater heat increment than has glucose.

9. Only 20 per cent of ingested xylose was recovered in the excreta of seven male rats on a 10-day balance study when measurement was made by formation of phloroglucide.

Only 32.52 per cent of ingested xylose was recovered in the excreta of seven male rats on a 10-day balance study when measurement was made of the energy of excreta of these animals as compared with pair mates fed an equal quantity of a 20 per cent glucose diet after allowance was made for the fecal and urinary nitrogen excreted.

Even if all the extra energy of the excreta were used as a basis for estimation of excreted xylose, only 45 per cent of that ingested was recovered.

Conclusions

It has been concluded from the evidence presented that there is no energy available from pure xylose when administered to the albino rat as a carbohydrate source in an other-

wise complete diet. A large percentage of ingested xylose was not recovered is the excreta. Precisely what occurs metabolically to the ingested pentose which cannot be recovered remains undetermined.

Ingestion of xylose creates albuminous degeneration of liver and kidney tissue which appears to be reversible. Its metabolic presence reduces the voluntary activity of the rat which may be a measure of toxicity.

There was no evidence of a change in the metabolic rate as a result of feeding xylose.

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